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EXAMINER	
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ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,323	BOLLA ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	mail

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-41 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-41 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 6/28/2006 in which claims 1-28 and 42 were cancelled; and claims 29, 37 and 43 were amended. Claims 29-41 and 43 are pending and under examination in the instant Office action.

Election/Restrictions

Applicant's traversal of the restriction requirement mailed 2/10/2006 is acknowledged. Applicant traverses the restriction requirement on the grounds that, to the extent it could be understood, the requirement is not in line with what Applicant regards as the invention. Applicant has further amended the claims so as to more closely reflect Applicant's invention and so as to alter claim dependency such that "[a]s amended, Claim 43 is not independent and distinct from the rest of the claims" (see page 4, paragraphs 3-5 of the remarks filed 6/28/2006).

Applicant's arguments and amendments have been carefully considered and Examiner has agreed to rejoin Groups I-IV of the restriction requirement.

Drawings

The drawings were received on 12/8/2003. These drawings are not acceptable.

In addition to Replacement Sheets containing the corrected drawing figure(s), Applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as "Annotated Sheets" and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d)(1). Failure to timely submit the proposed drawing and marked-up copy will result in the abandonment of the application.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

Replacement Drawing Sheets

Drawing changes must be made by presenting replacement sheets which incorporate the desired changes and which comply with 37 CFR 1.84. An explanation of the changes made must be presented either in the drawing amendments section, or remarks, section of the amendment paper. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). A replacement sheet must include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of the amended drawing(s) must not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective

action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and within the top margin.

Annotated Drawing Sheets

A marked-up copy of any amended drawing figure, including annotations indicating the changes made, may be submitted or required by the examiner. The annotated drawing sheet(s) must be clearly labeled as "Annotated Sheet" and must be presented in the amendment or remarks section that explains the change(s) to the drawings.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability.

Claim Objections

Claim 36 is objected to because of the following informalities: Claim 36 recites, "[t]he transformed yeast strain of claim 29 wherein said promoter is selected from the group consisting of AOX1, GAP, FLD1, PEx8, YP71, and GAPDH"

(emphasis added) in lines 1-2. The claim should instead recite "[t]he transformed yeast strain of claim 29 wherein said promoter is selected from the group consisting of AOX1, GAP, FLD1, PEx8, ~~YP71~~YPT1, and GAPDH". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-32, 37 and 39-41, and therefore dependent claims 33-36, 38 and 43, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is vague and indefinite in that the metes and bounds of a "yeast derived promoter" (line 2) are unclear. What are the steps performed in the deriving? What characteristics must be retained such that a promoter is "yeast derived?"

Claims 29 and 37 recite a "transformed yeast strain" that is "mixed in quantity with the predetermined feed source." Claims 29 and 37 are vague and indefinite in that it is unclear

what quantity of yeast must be mixed such that it is "in quantity" with the predetermined feed source. Is any quantity encompassed or does Applicant intend, e.g., equal parts yeast to feed source?

The term "optimum" in claims 29 and 37 is a relative term which renders the claim indefinite. The term "optimum" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Does Applicant intend that "optimum" dietary needs are those which result in phenotypes desirable for raising animals for slaughter, or are "optimum" dietary needs met when specific amino acids are provided in a particular weight percent as compared to lysine?

Claim 30 recites "[t]he transformed yeast strain of claim 29, whereby said strain is inducible" in lines 1-2. Claim 30 is vague and indefinite because it is not clear whether Applicant intends such a strain wherein the promoter is inducible, or whether Applicant intends that the strain itself is inducible, e.g., can be induced to proliferate upon incubation with a particular growth factor.

Claim 31 recites "[t]he transformed yeast strain of claim 29, whereby said nucleic acid polymer is inserted into said

strain's chromosome and said nucleic acid polymer is homozygous" in lines 1-2. Claim 31 is vague and indefinite in that it is unclear how the polynucleotide can be both "homozygous" as recited in claim 31 and can still encode a polypeptide "ordinarily exogenous to yeast" as recited claim 29. Is the nucleic acid polymer inserted into said strain's chromosome twice, thus making it homozygous? Or does Applicant intend the transformed yeast strain comprising a nucleic acid polymer of claim 29, wherein the nucleic acid polymer does NOT encode a protein ordinarily exogenous to the yeast?

Claim 32 recites "[t]he transformed yeast of claim 29, whereby said polypeptide is held by said strain" in lines 1-2. Claim 32 is vague and indefinite in that it is not clear what "held by" means. Does Applicant intend a transformed yeast cell of claim 29, wherein said polypeptide is not secreted, or does Applicant intend such a yeast cell wherein the polypeptide is stable within the cytoplasm of the yeast cell, or both?

Claim 39 recites "[t]he construct of claim 37 wherein said gene, when expressed, results in a polypeptide for poultry comprising: 6 Lysine, 3 Methionine/Cysteine; 2 Threonine; 1 Valine; 2 Isoleucine; 6 histidine; and 1 Tryptophan amino acid residues" in lines 1-3. Claim 39 is vague and indefinite because it is unclear whether Applicant intends 3 Methionine or

3 Cysteine residues, or whether Applicant intends 3 residues, wherein the residues are either Methionine or Cysteine in any combination.

Similarly, claims 40 and 41 recite "3 Methionine/Cysteine" and "2 Methionine/Cysteine" residues, respectively. These claims are also vague and indefinite in that it is unclear whether Applicant intends 3 (or 2) Methionine or 3 (or 2) Cysteine residues, or whether Applicant intends 3 (or 2) residues, wherein the residues are either Methionine or Cysteine in any combination.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-41 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a construct for insertion into a host cell comprising a gene having a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, said nucleic acid polymer having a sequence that codes for expression of one or more amino acid residues in a ratio that complements a predetermined feed source for a target animal, where the predetermined feed source is insufficient to meet optimum dietary needs of the target animal and the ratio is designed to offset the insufficiency when the construct is used to transfect a transformed yeast strain that is then mixed in quantity with the predetermined feed source for consumption by the target animal. The claims are further drawn to yeast transformed with such a construct and a method of producing a yeast additive for use in animal feed comprising inserting such a construct into a yeast strain and producing the encoded polypeptide. Some claims are further drawn to such a construct wherein the construct comprises a particular promoter such as a GAPDH promoter or a yeast-derived promoter. Some claims are further drawn to such a construct wherein the polypeptide encoded comprises particular amino acids (e.g. 10 lysine and 3 methionine/cysteine residues). The claims encompass any nucleic acid construct and/or any yeast cell transformed with such a construct wherein the normally exogenous polypeptide made

includes one or more amino acid residues that complement any predetermined feed source for any target animal as long as the predetermined feed source is insufficient to meet the optimum dietary needs of the target animal and the ratio is designed to offset the insufficiency. The claims do not provide any structural information with regard to the ratios of amino acids required and how such ratios would be determined such that it would complement an insufficiency in a predetermined feed source. The claims also do not provide any structural information regarding which target animals would be used with which ratios and predetermined feed sources such that the transformed yeast additive would offset in the insufficiency in the diet. Thus, the rejected claims comprise a set of nucleic acid sequences, ratios, predetermined feed sources and target animals that are defined by the function of the encoded protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes ratios of amino acids that "would approximate the

needed essential amino acids in corn based diets" for poultry, swine and dairy beef (see Example 9, pages 41-42; and Table 1). The specification also teaches "Ideal Indispensable Amino Acid Profiles (% of Lysine) of a Diet for Broiler Chicks in Two Age Categories (see Table 2, page 42) as well as "Metabolizable Amino Acid Requirements (grams/day) for Steers Gaining 2.3 kg per day at Two Body Weights" (see Table 4, page 44). As its sole working example, the specification describes the construction of a *Saccharomyces cerevisiae* strain transformed with a synthetic peptide inserted into the pGAPZb vector comprising a GAP promoter from *Pichia pastoris*. The synthetic peptide comprises histidine residues. However, no sequence information is provided with regard to the synthetic peptide except that it was generated by a 68 bp DNA product (page 46, first paragraph) and that it comprised histidine recognizable by an anti-histidine antibody (page 47, lines 8-15). Neither is any description provided of a single transformed yeast strain expressing a protein wherein the polypeptide or the yeast itself (comprising the proper ratio of amino acids), when mixed "in quantity" with a predetermined feed source, is utilized to offset an insufficiency in the optimum dietary needs of a single target animal.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of one transformed yeast strain. The results are not predictive of any other yeast strains/nucleic acids capable of being produced by a yeast such that the ratio of amino acids, when added to a predetermined feed source, is sufficient to offset the deficiency in the predetermined feed source. Thus it is impossible to extrapolate from the example described herein those nucleic acid molecules/amino acid ratios/predetermined feed sources/target animals that would necessarily meet the structural/functional characteristics of the rejected claims.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of genes or transformed yeast hosts that produce proteins with amino acid ratios that, when added to a predetermined feed source "in quantity" will result in the offset of a deficiency in the optimum dietary needs for a target animal. The literature contains many examples of yeast transformed to express polypeptides comprising certain amino acids (see, e.g., Tully et al, US Patent No. 6,337,193; Cheng et al, US Patent No. 5,985,605; and Lei US Patent No. 6,451,572). For example, Cheng et al (US Patent No. 5,985,605) teach the use of recombinant

yeast strain which can be used as animal feed but they do not describe such a yeast strain or such a method such that the amino acid ratio provided by the yeast strain complements a diet from a predetermined feed source such that it offsets the deficiency of the predetermined feed source in a target animal.

Given the very large genus of nucleic acid molecules encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the chimeric sequences capable of fulfilling the claim limitations of claims 29-41 and 43, the skilled artisan would not have been able to describe the broadly claimed genus of nucleic acid constructs, transformed yeast comprising such constructs or methods of use of such constructs such that the amino acid ratio complements a predetermined feed source for a target animal where the predetermined feed source is insufficient to meet optimum dietary needs of the target animal. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those nucleic acid sequences/transformed yeast constructs used in combination with predetermined feed sources and target animals that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have

reasonably concluded Applicant was not in possession of the claimed invention for claims 29-41 and 43.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 29, 37 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Nussenzweig et al (US Patent No. 4,826,957).

Note: For purposes of this rejection, the intended use of the nucleic acid polymer for expression of one or more amino acid residues in a ratio that complements a predetermined feed source for a target animal, wherein the predetermined feed source is insufficient to meet optimum dietary needs of the target animal and the ratio is designed to offset the

insufficiency when the transformed yeast strain in mixed in quantity with the predetermined feed source for consumption by the target animal is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter since any such yeast cell could fulfill the claim limitations wherein the optimum dietary needs are determined to be fulfilled and complemented by the particular exogenous protein produced by the transformed yeast, whatever that protein may be.

Nussenzweig et al teach a transformed yeast strain (*Saccharomyces cervisiae* strain AB110) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (*P. vivax* circumsporozoite protein antigen) under the control of a yeast derived promoter (an ADH-GAPDH promoter hybrid), said nucleic acid polymer being a synthetic polymer (see entire document, especially Example 1 at column 9, lines 40-45; and column 10, lines 9-68). Nussenzweig et al also teach such a nucleic acid construct for insertion into a host yeast and a method for producing a yeast additive comprising inserting such a construct into a yeast strain and expressing the gene in said construct (ibid).

Claims 29-30, 32, 34-37, 39-41 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Tully et al (US Patent No. 6,337,193).

Note: For purposes of this rejection, the intended use of the nucleic acid polymer for expression of one or more amino acid residues in a ratio that complements a predetermined feed source for a target animal, wherein the predetermined feed source is insufficient to meet optimum dietary needs of the target animal and the ratio is designed to offset the insufficiency when the transformed yeast strain in mixed in quantity with the predetermined feed source for consumption by the target animal is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter. This is because any such yeast cell could fulfill the claim limitations wherein the optimum dietary needs are determined to be that which is fulfilled by the composition of the exogenous protein produced.

Tully et al teach a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially Figures 2 & 5; column 2, lines 5-12

& 20-28; column 3, lines 18-36; and column 5, lines 40-45). Tully et al teach such a strain wherein the strain is inducible, i.e., wherein the production of the MBP protein is under the control of the AOX1 promoter which is inducible by methanol (see, e.g., column 5, lines 20-25). Regarding claim 32, the polypeptide produced by the transformed yeast is "held" by the transformed yeast insofar as even transformed cells that secret the protein would "hold" the protein for a given period of time before the protein is released into the culture medium. Regarding claim 34, the transformed yeast strain is *Pichia pastoris* (see, e.g., column 2, line 26-28). Regarding claim 35, the transformed yeast produces a protein comprising 3 methionine, 6 histidine, 6 lysine, 2 threonine, 2 isoluecine, 1 valine and 1 tryptophan residues (see, e.g., the human PDI gene sequence found in Figure 2). Regarding claim 36, the promoter utilized for the production of PDI is the GAPDH promoter (see, e.g., column 5, lines 15-45). Regarding claims 37 and 39-41, Tully et al also teach the construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein the nucleic acid polymer is a plasmid and is used to make a protein that would be capable of complementing a deficiency in predetermined feed source wherein the expressed

protein results in a polypeptide comprising 6 lysine, 3 methionine/cystein, 2 threonine, 1 valine, 2 isoleucine, 6 histidine and 1 tryptophan residues (claim 39); wherein the expressed protein results in a polypeptide comprising 10 lysine and 3 methionine/cysteine residues (claim 40); and wherein the expressed protein results in a polypeptide comprising 10 lysine, 2 methionine/cysteine, 10 arginine and 3 histidine residues (the PDI gene found in Figure 2 meets all of the preceding amino acid requirements). Tully et al also teach a method for producing this yeast additive comprising inserting such a construct into a yeast strain and expressing the gene (see, e.g., Example 3, columns 11-14).

Claims 29-30, 32-34, 36-37 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheng et al (US Patent No. 5,985,605).

Note: For purposes of this rejection, the intended use of the nucleic acid polymer for expression of one or more amino acid residues in a ratio that complements a predetermined feed source for a target animal, wherein the predetermined feed source is insufficient to meet optimum dietary needs of the target animal and the ratio is designed to offset the insufficiency when the transformed yeast strain in mixed in

quantity with the predetermined feed source for consumption by the target animal is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter. This is because any such yeast cell could fulfill the claim limitations wherein the optimum dietary needs are determined to be that which is fulfilled by the composition of the exogenous protein produced.

Cheng et al teach a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (*Selenomonas ruminantium* JY35 phytase) under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially Figures 15; column 5, lines 54-58; column 3, lines 66-67 through column 4, lines 1-15; and column 7, lines 44-65). Cheng et al teach such a strain wherein the strain is inducible (see, e.g., column 9, lines 11-36). Regarding claim 32, the polypeptide produced by the transformed yeast is "held" by the transformed yeast insofar as the transformed cells may or may not secrete the exogenous protein (see, e.g., column 7, lines 57-59). Regarding claim 34, the transformed yeast strain is *P. pastoris* or *S. cerevisiae* (see, e.g., column 7, line 44-49). Regarding claim 36, a promoter utilized for the production of phytase is

the GAPDH promoter (see, e.g., column 8, lines 9-18). Regarding claims 37 and 39-41, Cheng et al also teach the construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein the nucleic acid polymer is a plasmid and is used to make a protein that would be capable of complementing a deficiency in predetermined feed source wherein the expressed protein results in a polypeptide comprising 6 lysine, 3 methionine/cystein, 2 threonine, 1 valine, 2 isoleucine, 6 histidine and 1 tryptophan residues (claim 39); wherein the expressed protein results in a polypeptide comprising 10 lysine and 3 methionine/cysteine residues (claim 40); and wherein the expressed protein results in a polypeptide comprising 10 lysine, 2 methionine/cysteine, 10 arginine and 3 histidine residues (the phytase gene found in Figure 15 meets all of the preceding amino acid requirements). Cheng et al also teach a method for producing this yeast additive comprising inserting such a construct into a yeast strain and expressing the gene (see, e.g., column 12, lines 56-67 and column 13, lines 1-9).

Claims 29-30, 32-34, 36-37 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Lei (US Patent No. 5,985,605).

Note: For purposes of this rejection, the intended use of the nucleic acid polymer for expression of one or more amino acid residues in a ratio that complements a predetermined feed source for a target animal, wherein the predetermined feed source is insufficient to meet optimum dietary needs of the target animal and the ratio is designed to offset the insufficiency when the transformed yeast strain in mixed in quantity with the predetermined feed source for consumption by the target animal is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter. This is because any such yeast cell could fulfill the claim limitations wherein the optimum dietary needs are determined to be that which is fulfilled by the composition of the exogenous protein produced.

Lei teaches a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (see, e.g., the appA gene of *E.*coli at column 5, lines 63-64) under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially

column 5, lines 45-67; column 6, lines 33-37; and column 8, lines 9-56). Lei teaches such a strain wherein the strain is inducible (see, e.g., column 8, lines 11-36). Regarding claim 32, the polypeptide produced by the transformed yeast is "held" by the transformed yeast insofar as the transformed cells do not secrete the exogenous protein (see, e.g., column 7, lines 19-24). Regarding claim 33, the transformed yeast cell is auxotrophic, but was non-auxotrophic prior to transformation, as would be the case with the use of URA3 as a selectable marker (see, e.g., column 8, lines 50-56). Regarding claim 34, the transformed yeast strain is *S. cerevisiae* (see, e.g., column 6, lines 3-37). Regarding claim 36, a promoter utilized for the production of phytase is the GAPDH promoter (see, e.g., column 8, lines 9-18). Regarding claims 37, Lei also teaches the construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein the nucleic acid polymer is a plasmid and used to make a protein that would be capable of complementing a deficiency in predetermined feed source when added in quantity to the predetermined feed source for consumption by the target animal (see, e.g., column 7, lines 36-67 and column 8, lines 1-28). Lei also teaches a method for producing this yeast additive comprising inserting such a

construct into a yeast strain and expressing the gene (see, e.g., Example 4 at column 16 and Example 7 at column 20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29-30, 32-34, 36-38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lei (cited above) in view of Sikorski et al (*Genetics* **122**:19-27, 1989).

As explain above, Lei teaches a nucleic acid construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein the nucleic acid polymer is a plasmid and is used to make a protein that would be capable of complementing a deficiency in predetermined feed source when added in quantity to the predetermined feed source for consumption by the target animal (see, e.g., column 7, lines 36-67 and column 8, lines 1-28). Lei also teaches a method for producing this protein comprising inserting such a construct into a yeast strain and expressing the gene (see, e.g., Example 4 at column 16 and Example 7 at column 20). Regarding the use of vector, Lei teaches that the vector can be any vector that replicates autonomously or integrates into the genome of the yeast. Lei also teaches that the promoter may be a glyceraldehydes-3-phosphate dehydrogenase promoter (see column 7, last paragraph and column 8, first full paragraph). Lei also

teaches the use of vectors which carry URA3 as a selectable marker.

Lei does not teach such a construct wherein said construct is a pRS316 plasmid with a GAPDH promoter.

Sikorski et al teach the use of the pRS316 plasmid for expression of proteins in yeast. Sikorski et al teach that pRS316 comprises the URA3 selectable marker and that such a vector has the advantage that "in addition to the general features afforded the pRS vectors by the pBLUESCRIPT backbone, such as ssDNA production, high plasmid DNA yields and extensive polylinker, unidirectional deletion formation and simplified cloning (blue/white screening for recombinants), these new vectors offer unique yeast-specific features," i.e., the pRS316 vectors "allow one to perform almost all routine yeast DNA manipulations in the same plasmid" (see page 25, 2nd column, first full paragraph). Sikorski et al also teach that the streamlined design of the pRS vectors makes them well suited to serve as the starting point for construction of other yeast vectors (see entire document, especially paragraph briding pages 24-25 and page 25, second column, first full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the pRS316 vector as taught by Skorski et al with the GAPDH promoter as

taught by Lei, because Lei teaches the use of any yeast vector for production of a heterologous protein in yeast and and further teaches the use of a GAPDH promoter for expression of the protein and the use of a URA3 selectable marker;Sikorski et al teach that pRS316 is a useful vector for maninupaltion of DNA (such as cloning) and expression of proteins in yeast and that it comprises a URA3 selectable marker.

One would have been motivated to substitute the pRS316 vector as taught by Sikorski et al in the methods taught by Lei, including the use of the GAPDH promoter, because Sikorski et al teach that the streamlined design of the pRS vectors would make DNA manipulations and cloning easier and Lei teaches that the use of the GAPDH promoter for strong production of a heterologous protein in yeast and the URA3 marker for selection.

Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when utilizing the pRS316 yeast vector as taught by Sikorski et al in the methods and constructs as taught by Lei.

Conclusion

No claim is allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

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September 12, 2006

NANCY VOGEL
PRIMARY EXAMINER